LABELING

*angio*LINK

Vascular Closure System

Instructions for Use

IMPORTANT!

This booklet is designed to assist in using the EVS ™ Vascular Closure System. It is not a reference to surgical techniques. To ensure proper use of this device and to prevent injury to patients, read all information contained in these instructions for use.

CAUTION:

Federal law (USA) restricts this device to sale by or on the order of a physician.

FOR SINGLE USE ONLY; DO NOT RE-STERILIZE OR REUSE THIS DEVICE.

INDICATIONS FOR USE

The EVS™ Vascular Closure System is indicated for "Percutaneous Femoral Artery Approximation". The EVS™ Vascular Closure System is also indicated to reduce time to hemostasis at a femoral puncture site and to reduce time to ambulation for patients undergoing diagnostic or interventional catheterization procedures using 6 - 8 French procedural sheaths.

CONTRAINDICATIONS:
There are no known contraindications for the EVS™ Vascular Closure System.

DEVICE DESCRIPTION

The EVS™ Vascular Closure System is designed to deliver a titanium staple to close 6Fr. - 8Fr. artery puncture sites following diagnostic or interventional procedures.

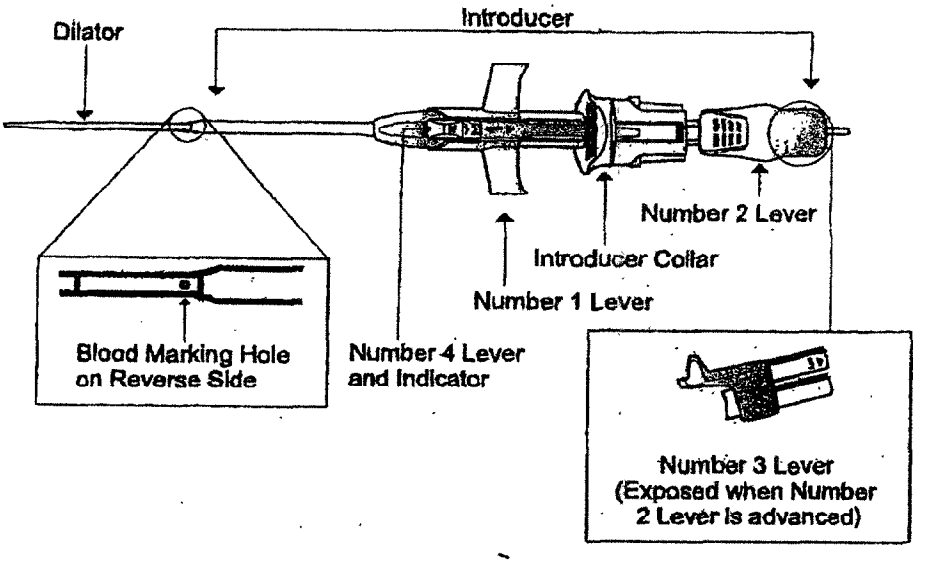
The staple material is radiopaque.

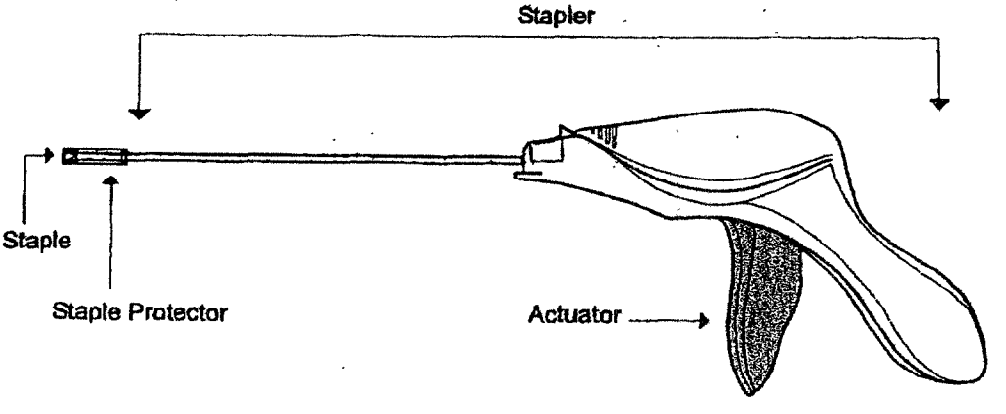
This device achieves hemostasis by mechanical means of approximating the arteriotomy end to end, and then delivering an extraluminal staple to effect the repair of the arteriotomy.

HOW SUPPLIED

Includes one (1) introducer with integrated vessel stabilizers and dilator, compatible with .038 or smaller guide-wires.

Includes one (1) stapler with one pre-loaded staple.





WARNINGS

- Do not use to close arteriotomies created through a vascular graft.
- Avoid use of the EVS™ Vascular Closure System if bacterial contamination of the sheath or surrounding tissue may have occurred.
- Do not use in ischemic or necrotic tissue because it could tear the vessel.

PRECAUTIONS

- Do not use if package is damaged or any portion of the package has been previously opened.
- Do not use if the items in the package appear to be damaged or defective in any way.
- The EVS™ is to be used only by a trained, licensed physician or healthcare professional.
- If a patient has had a procedural sheath left in place for longer than 8 hours, consideration should be given to the use of prophylactic antibiotics prior to utilizing the EVS™ Vascular Closure System.
- When a venous sheath has been placed in the same leg as the arterial sheath, the venous sheath should be removed and hemostasis obtained prior to use of the EVS™ Vascular Closure System.
- The stapler handle levers must be squeezed together firmly as far as they will go or the staple may not be fully released from the device. Failure to squeeze the lever of the stapler completely can result in the misfiring of the staple and incomplete release of the vessel wall by the introducer.
- Inspect the access site to ensure proper application. If hemostasis is not achieved after application, apply compression for two (2) minutes.
- Use conventional compression methods in the event bleeding from the femoral access site persists after the use of the EVS™ Vascular Closure System.
- The location of the staple should be verified using flouroscopy, if in question.
- Do not re-sterilize or reuse this product; it is intended for a SINGLE USE ONLY.

Before considering discharge, assess the patient for the following clinical conditions:

- Conscious sedation
- Unstable cardiac status
- Hematoma at the closure site
- Hypotension
- Pain while walking
- Bleeding at the closure site
- Any co-morbid condition requiring observation

The presence of the above factors has generally led to deferral of discharge recommendations.

SPECIAL PATIENT POPULATIONS

The safety and effectiveness of using the EVS™ Vascular Closure System has not been established in the following patient populations:

- Patients who are ≤ 18 or ≥ 80 years of age.
- Patients with pre-existing autoimmune disease.
- Patients with a history of bleeding disorder/platelet disorder such as Von Willebrand's disease or hemophilia.
- Presence of bilateral chronic ischemia identified by bilateral claudication and significant atherosclerotic disease at the site of, or immediately adjacent to the site of, sheath insertion as determined by screening femoral angiography.
- Patients undergoing thrombolytic therapy administered 24 hours prior to the catheterization procedure.
- Patients having previous femoral vascular surgery at the targeted site.
- Patients with a stent placed in the vicinity of the arterial puncture site.
- Patient with pre-existing arterio-venous fistula at targeted site.
- Patients with pre-existing non-cardiac systemic disease or terminal illness.
- Patients with pre-existing systemic or cutaneous infection.
- Patients with pre-existing ipsilateral groin hematoma.
- Patients that could not be accessed with a standard needle (i.e., Seldinger needle).
- Patients with failed single wall arterial puncture.
- Patients with bleeding around sheath prior to sheath removal.
- Patients with absent pedal pulses of either extremity.
- Patients with tortuous vascular anatomy with greater than 90° bends.
- Patients experiencing cardiogenic shock during or immediately post-procedure.
- Patients with procedural usage of Angiomax™ anticoagulant therapy.
- Patients undergoing catheterization procedures using < 6Fr. and > 8Fr. procedural sheaths.

ARTERIAL PUNCTURE CONSIDERATIONS

Percutaneously puncture the anterior wall of the common femoral artery, superficial femoral artery, or profundus femoral artery optimizing placement below the inguinal ligament at an angle of approximately 45 degrees.

ADVERSE EVENTS

The EVS™ Vascular Closure System was evaluated in a pivotal, prospective, multi-center, open-label, randomized study involving 362 patients. The EVS™ Vascular Closure System was compared to manual compression methods following interventional and diagnostic cardiac and peripheral vascular procedures with 8 Fr or smaller sheath sizes. Of the 362 randomized patients, 243 (67%) were randomized to the EVS™ Vascular Closure System and 119 (33%) were randomized to manual compression. Randomized EVS™ patients were approximately evenly divided between the procedure groups: 118 (49%) had interventional procedures and 125 (51%) had diagnostic procedures.

Patients who were randomized to the EVS™ device were asked to ambulate at pre set time intervals after the diagnostic/interventional procedure was complete. EVS™ patients without IIb/IIIa inhibitors were ambulated at 1 hour, while patients with IIb/IIIa inhibitors were ambulated at 2 hours.

The study was designed to detect a difference in the observed cumulative incidence of major complications at 30 days. Assuming a 3% cumulative major complication rate for manual compression, the study was designed to rule out a 5% higher major complication rate for the randomized EVS™ group. The sample size was adequate to rule out a 5% EVS™ disadvantage using a 95% upper confidence bound.

The EVS™ device demonstrated safety. By Day 30, a cumulative total of 1 (0.4%) major complication was reported for randomized patients who received EVS™ compared to 3 (2.5%) major complications in the manual compression patients.

Minor complication rates were similar between randomized EVS™ and manual compression patients (8.7% and 8.3%, respectively).

Table 1: Cumulative Anticipated Major and Minor Complications (ITT Population)

	Received EVS (N=243)		Received MC (N=119)		Fisher's Exact Test P-value[1]
	No. (%) of Patients	No. of Events	No. (%) of Patients	No. of Events	
Combined major complications at Day 30[2]	1 (0.4%)	1	3 (2.5%)	3	0.1058
Retroperitoneal bleeding	1 (0.4%)	1	1 (0.8%)	1	0.5500
Uncontrolled bleeding requiring transfusion	0 (0.0%)	0	1 (0.8%)	1	0.3287
New ischemia in ipsilateral leg	0 (0.0%)	0	1 (0.8%)	1	0.3287
Ultrasound guided compression for vascular surgery	0 (0.0%)	0	0 (0.0%)	0	
Vascular Surgery	0 (0.0%)	0	0 (0.0%)	0	
Intraluminal staple delivery requiring surgical intervention	0 (0.0%)	0	0 (0.0%)	0	
Groin related infection requiring IV antibiotics or extended hospitalization	0 (0.0%)	0	0 (0.0%)	0	
New significant neuropathy in ipsilateral lower extremity	0 (0.0%)	0	0 (0.0%)	0	
Total Vessel Occlusion	0 (0.0%)	0	0 (0.0%)	0	
Combined minor complications at Day 30	22 (9.1%)	31	9 (7.6%)	13	0.6941
Uncontrolled bleeding not requiring transfusion	3 (1.2%)	3	3 (2.5%)	3	0.3992
Hematoma ≥6cm	9 (3.7%)	11	4 (3.4%)	5	1.0000
Ecchymosis >3mm	11 (4.5%)	11	5 (4.2%)	5	1.0000
Intraluminal staple delivery not requiring surgical intervention	1 (0.4%)	1	0 (0.0%)	0	1.0000
Pseudoaneurysm not requiring treatment	3 (1.2%)	3	0 (0.0%)	0	0.5538
Pseudoaneurysm requiring thrombin injection	2 (0.8%)	2	0 (0.0%)	0	1.0000
Pedal pulse diminished by ≥ 2 grades	0 (0.0%)	0	0 (0.0%)	0	
Ipsilateral lower extremity arterial emboli	0 (0.0%)	0	0 (0.0%)	0	
Ipsilateral deep vein thrombosis	0 (0.0%)	0	0 (0.0%)	0	
Access site-related vessel laceration	0 (0.0%)	0	0 (0.0%)	0	
Access site wound dehiscence	0 (0.0%)	0	0 (0.0%)	0	
Localizes access site infection treated with intramuscular or oral antibiotics	0 (0.0%)	0	0 (0.0%)	0	
Arteriovenous fistula	0 (0.0%)	0	0 (0.0%)	0	

[1] Based on the comparison of the percentage of patients who experienced major or minor complications between the EVS and MC groups.

[2] The number of patients with a major complication or a specific type of major complication is equal to the number of major complication events. Each patient only experienced a given major complication once.

CLINICAL TRIAL

The effectiveness of the EVS™ Vascular Closure System was evaluated using two primary endpoints: time to hemostasis and time to ambulation. Time to hemostasis was defined as the time from staple delivery to the time total cessation of bleeding (including any oozing) was achieved. Time to ambulation was defined as the time from staple delivery to the time the patient stands at bedside and walks no less than 20 feet in total distance.

Use of EVS™ significantly reduced time to hemostasis and ambulation. The mean time to hemostasis was 4.4 minutes for randomized EVS™ patients, compared to 20.7 minutes for manual compression patients. The mean time to ambulation was 2.4 hours for randomized EVS™ patients compared to 6.0 hours for MC patients.

Table 2: Descriptive Statistics for Effectiveness (ITT Population)

	Randomized EVS (N=243)	Randomized MC (N=119)	P-value
Time to hemostasis (minutes)			<0.0001[1]
N	222	116	
Mean (SD)	4.4 (4.1)	20.7 (8.0)	
Median	3.0	20.0	
Min-Max Range	0.0 – 25.0	2.0 – 62.0	
Time to ambulation (hours)			<0.0001[1]
N	214	103	
Mean (SD)	2.4 (3.3)	6.0 (5.2)	
Median	1.3	4.6	
Min-Max Range	0.8 – 24.2	2.9 – 44.5	
Time to Eligible Hospital Discharge (hours)			0.5382[1]
N	203	98	
Mean (SD)	20.1 (31.1)	18.1 (25.4)	
Median	8.5	6.6	
Min-Max Range	1.1 – 271.8	0.7 – 141.5	
Time to Actual Hospital Discharge (hours)			0.2053[1]
N	225	110	
Mean (SD)	23.0 (35.8)	19.0 (21.3)	
Median	13.6	9.5	
Min-Max Range	1.3 – 311.0	0.7 – 146.0	
Time from end of procedure to device deployment (minutes)			<0.0001[1]
N	243	118	
Mean (SD)	7.9 (21.4)	76.7 (110.5)	
Median	6.0	22.5	
Min-Max Range	0.0 – 330.0	0.0 – 723.0	
Time from sheath removal to device deployment (minutes)			<0.0001[1]
N	243	118	
Mean (SD)	1.3 (2.2)	0.2 (0.9)	
Median	1.0	0.0	
Min-Max Range	-2.0 – 16.0	0.0 – 6.0	

[1] p-value based on an unpaired t-test comparing randomized EVS and MC subjects.

Table 3: Descriptive Statistics for Effectiveness in Subjects Undergoing Diagnostic and Interventional Procedures (ITT Population)

	Diagnostic Randomized EVS (N=125)	Diagnostic Randomized MC (N=63)	P-value	Interventional Randomized EVS (N=118)	Interventional Randomized MC (N=56)	P-value
Time to hemostasis (minutes)			<0.0001[1]			<0.0001[1]
N	116	63		106	53	
Mean (SD)	3.3 (2.6)	19.3 (5.7)		5.5 (5.1)	22.3 (9.9)	
Median	2.5	20.0		4.0	20.0	
Min-Max Range	0.0 – 15.0	2.0 – 43.0		0.0 – 25.0	2.0 – 62.0	
Time to ambulation (hours)			<0.0001[1]			0.0004[1]
N	112	55		102	48	
Mean (SD)	1.5 (1.1)	4.7 (2.2)		3.4 (4.5)	7.6 (7.0)	
Median	1.2	4.3		2.0	5.6	
Min-Max Range	0.8 – 7.6	2.9 – 20.0		0.9 – 24.2	3.4 – 44.5	
Time to Eligible Hospital Discharge (hours)			0.8561[1]			0.2137[1]
N	102	57		101	41	
Mean (SD)	15.4 (36.4)	16.5 (29.6)		24.9 (23.8)	20.3 (18.0)	
Median	4.5	5.8		19.7	17.0	
Min-Max Range	1.1 – 271.8	0.7 – 141.5		1.4 – 147.3	1.5 – 79.1	
Time to Actual Hospital Discharge (hours)			0.4587[1]			0.2232[1]
N	113	58		112	52	
Mean (SD)	19.9 (46.1)	15.9 (24.9)		26.2 (20.4)	22.6 (15.8)	
Median	5.6	6.6		21.8	20.9	
Min-Max Range	1.3 – 311.0	0.7 – 146.0		2.1 – 119.4	4.7 – 74.7	

[1] p-value based on an unpaired t-test comparing randomized EVS and MC subjects.

Table 4: Kaplan-Meier Estimates of Patients Achieving Effectiveness Endpoints

Endpoint	Post-Procedure Time Interval	Randomized EVS (N=243)		Randomized MC (N=119)		Log Rank P-value
		No. Achieving Endpoint	%	No. Achieving Endpoint	%	
Time to hemostasis (minutes)						<0.0001
	≤ 1 min	40	16.94%	0	0.00%	
	≤ 5 min	167	71.55%	2	1.69%	
	≤ 10 min	208	89.65%	7	5.93%	
	≤ 15 min	216	93.57%	22	18.64%	
	≤ 20 min	218	94.70%	89	75.42%	
Time to ambulation (hours)						<0.0001
	≤ 1hr	35	14.77%	0	0%	
	≤ 2 hours	156	66.30%	0	0%	
	≤ 3 hours	184	78.71%	1	0.89%	
	≤ 4 hours	194	83.24%	20	17.70%	
	≤ 5 hours	197	84.63%	68	60.18%	
Time to eligible hospital discharge (hours)						0.5517
	≤ 1hr	0	0%	1	0.85%	
	≤ 2 hours	16	6.78%	2	1.69%	
	≤ 3 hours	26	11.01%	4	3.39%	
	≤ 4 hours	50	21.23%	8	6.78%	
	≤ 5 hours	67	28.53%	29	25.23%	
	≤ 10 hours	105	45.10%	56	49.27%	
	≤ 24 hours	161	71.06%	81	74.01%	
Time to actual hospital discharge (hours)						0.7301
	≤ 1hr	0	0%	1	0.84%	
	≤ 2 hours	8	3.33%	1	0.84%	
	≤ 3 hours	19	7.93%	1	0.84%	
	≤ 4 hours	35	14.66%	2	1.69%	
	≤ 5 hours	58	24.33%	19	16.46%	
	≤ 10 hours	109	45.77%	56	48.66%	
	≤ 24 hours	162	68.86%	85	74.68%	

Rates of device failure and operator error were low. There were 2 (0.8%) randomized EVS™ patients who experienced a device failure and 7 (2.9%) randomized EVS™ patients who experienced an operator error. The procedural success rate (the percentage of patients achieving hemostasis within 20 minutes minus the percentage with any major complications) was significantly higher in randomized EVS™ patients (94.4%) compared to manual compression (72.9%). EVS™ could be readily deployed without evidence of an investigator learning curve. Satisfactory puncture site healing at 30 days was achieved by 98.8% of randomized EVS™ patients and 96.6% of manual compression patients.

The majority of investigators reported that the use of the EVS™ was easier or as easy to use as other marketed devices, and that they had no difficulty or insignificant difficulty with the device set-up, operation, deployment, and function.

Table 5: Overall Performance of Device for all Sites (ITT Population)

	Randomized EVS (N=243)	Randomized MC (N=119)	p-value[1]
Procedural success			0.0001
Life-table estimate of hemostasis within 20 minutes [number of subjects]	94.7% [218]	75.4% [89]	
Minus major complication rate [number of subjects]	(0.4%) [1]	(2.5%) [3]	
Procedural success rate[2]	94.3%	72.9%	
Satisfactory puncture site healing (Day 30)			0.3971
Yes	240 (98.8%)	115 (96.6%)	
No	3 (1.2%)	3 (2.5%)	
Device failure			1.0000
Yes	2 (0.8%)	0 (0.0%)	
No	241 (99.2%)	119 (100.0%)	
Operator error			0.1008
Yes	7 (2.9%)	0 (0.0%)	
No	236 (97.1%)	119 (100.0%)	

[1] p-value based on Fisher's exact test comparing randomized EVS and MC subjects.
[2]The procedural success rate was defined as the percentage of subjects in the ITT population achieving hemostasis within 20 minutes minus the percentage with any major complications.

Table 6: ACT level prior to Sheath Removal (ITT Population)

	Randomized EVS (N=243)	Randomized MC (N=119)	Randomized EVS Diagnostic (N=125)	Randomized MC Diagnostic (N=63)	Randomized EVS Interventional (N=118)	Randomized MC Interventional (N=56)
ACT level (seconds) prior to sheath removal						
N	241	115	123	61	118	54
Mean (SD)	182.7 (65.2)	142.8 (34.0)	137.0 (43.0)	126.7 (35.0)	230.4 (47.8)	161.1 (21.8)
Median	179.0	154.0	129.0	123.0	232.0	162.0
Min-Max Range	63.0 – 427.0	42.0 – 229.0	63.0 – 311.0	42.0 – 180.0	65.0 – 427.0	103.0 – 229.0

Before the study, 49.4% of EVS™ patients (120/243) received anti-coagulant therapy, versus 39.5% of manual compression patients (47/119), while during the study 93.4% (227/243) of EVS™ patients received anti-coagulant therapy, compared to 90.8% of manual compression patients (108/119).

In addition to a difference between the treatment groups in the percentages of randomized patients who received anti-coagulant therapy, there was a notable difference in mean ACT levels at the time the procedural sheath was removed. Randomized EVS™ patients had a mean ACT at sheath removal of 182.7 seconds compared to 142.8 seconds for the manual compression group. For randomized subjects undergoing interventional procedures, the difference was more dramatic: interventional randomized EVS™ subjects had a mean ACT level of 230.4 seconds prior to sheath removal as compared to 161.1 seconds for MC subjects. ACT levels were higher at the time of sheath removal for EVS™ patients because the MC patients had delayed sheath removal while waiting for ACT levels to drop to clinically safe levels.

ANGIOLINK EVS™ VASCULAR CLOSURE SYSTEM INSERTION PROCEDURE

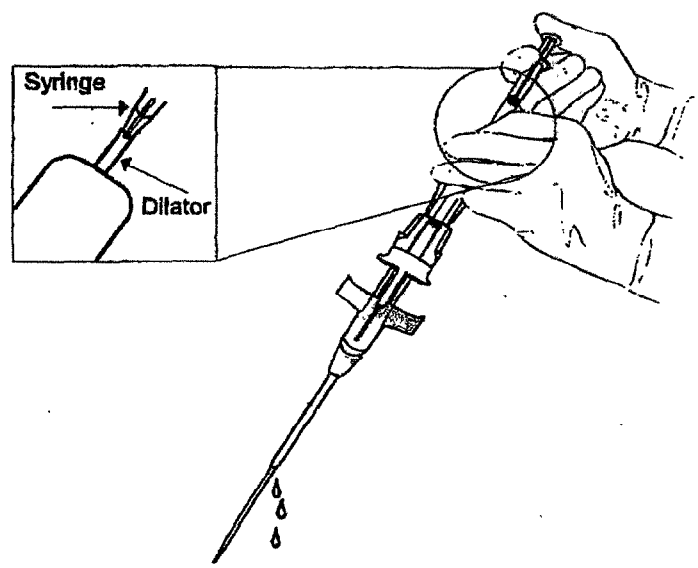
The EVS™ Vascular Closure System is to be used only by a licensed physician or other healthcare professional authorized by, or under the direction of such physician possessing adequate instruction in the use of the device.

Observe sterile technique at all times when using the EVS™ Vascular Closure System.

Follow physician orders regarding patient ambulation and discharge.

Repuncture at the site can be performed immediately after initial repair, if so indicated.

1. **Use a syringe to flush the blood marking hole with intravenous compatible fluid.**



2. **Create a skin nick to reduce friction at the skin level. Orient the introducer assembly so that the NUMBER 1 on the device is facing upward.**

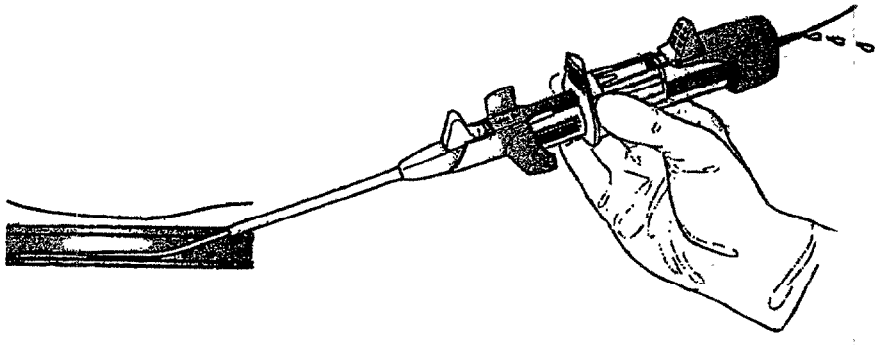
While resting the right hand on the patient's thigh, track slowly over a .038 or smaller guide wire using a low angle of approach. Gentle twisting as you track down helps achieve pulsatile blood marking. Avoid excessive forward pressure.

When blood marking is first achieved, the device may not be at its optimal location; depending on the patient's anatomy, the device may be pushed back slightly when forward pressure is released, causing optimal location to be lost.

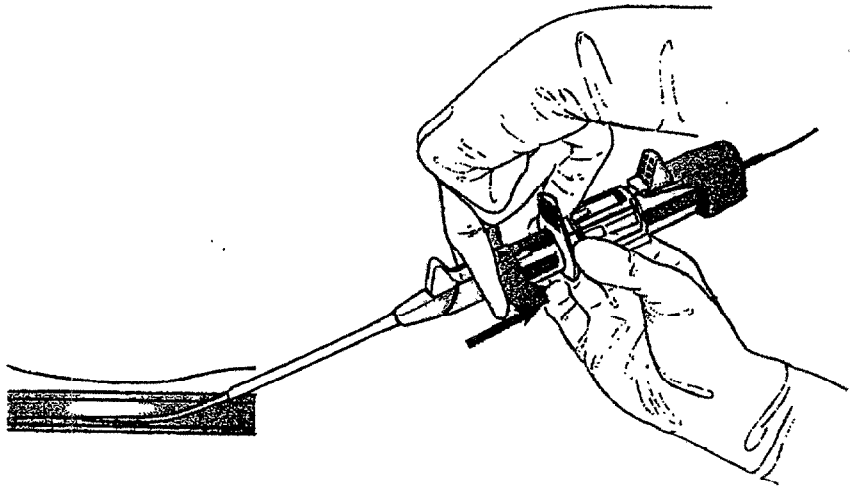
Gently twist and advance the introducer until blood marking is achieved and release forward pressure. If blood marking is lost or diminished upon releasing forward pressure, gently advance the introducer forward again until blood marking is re-achieved. Repeat this process until blood marking is maintained upon releasing forward pressure on the device.

3. When pulsitile blood marking has been achieved and maintained, **hold the introducer stable** with moderate forward pressure.

Do not allow the introducer to move forward or backward from this location until vessel stabilizers are fully retracted (step 6).

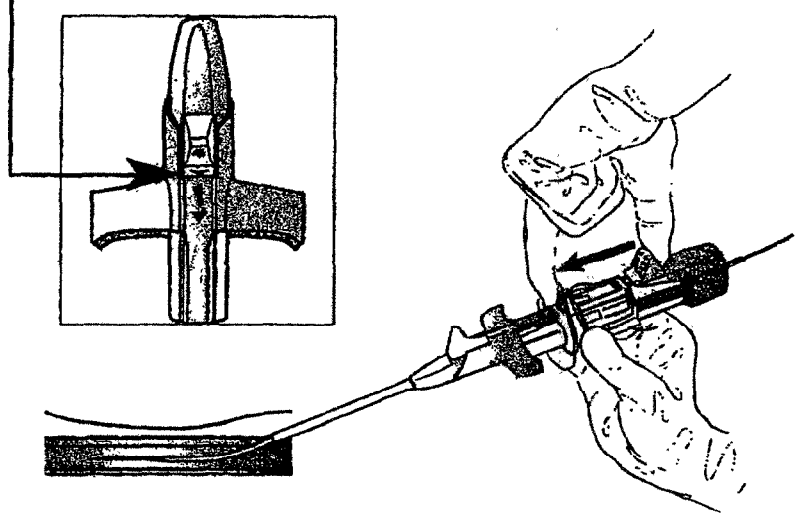


4. Pull back lever **NUMBER 1** to prepare the vessel stabilizers for deployment.

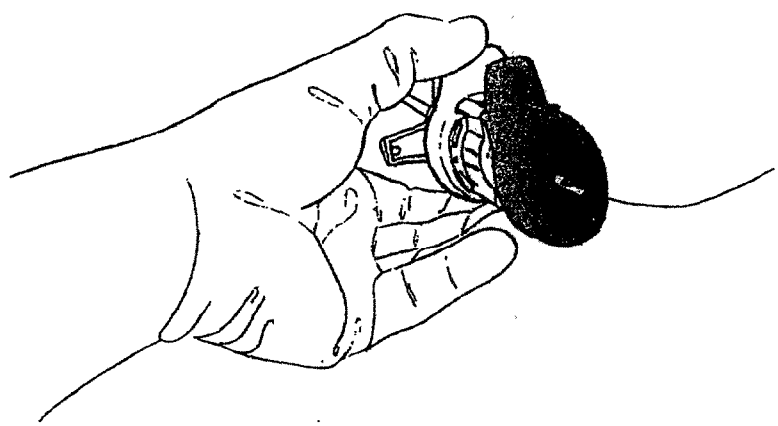


5. While maintaining the location of the introducer with moderate forward pressure, use your left hand to advance the **NUMBER 2** slide forward completely, until an audible click is heard. Remove left hand from the device allowing the now exposed number 3 lever to spring back from the introducer body.

If the lever marked **NUMBER 4** does not retract fully to the green indicator, gently advance it proximal to the device until green is the only color visible.



6. Maintain the introducer position while you switch control of the device from your right hand to your left hand. Hold the collar of the introducer as illustrated below.

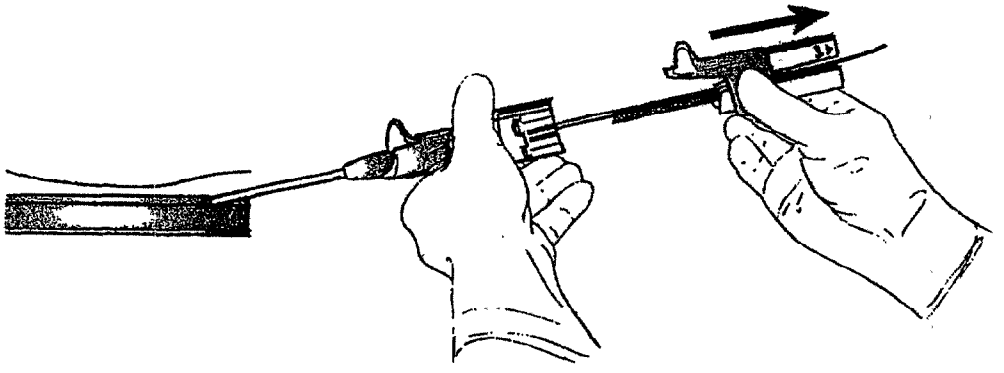


7. Maintain the introducer position. Remove the component marked with a **NUMBER 3** along with the guidewire.

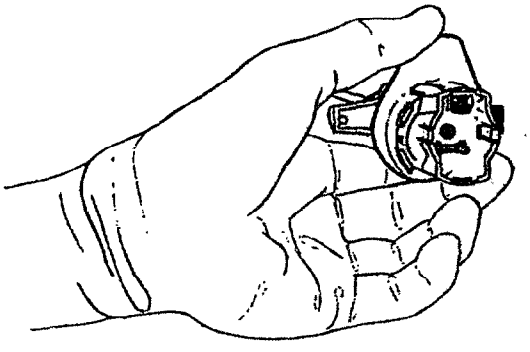
If the NUMBER 3 component cannot be removed, keep the guidewire in place. Firmly pull on the NUMBER 1 lever until a solid green block is clearly visible on the NUMBER 4 indicator. Remove the device and exercise one of the following options:

1. Track a new device over the wire and deploy as described in steps 1-7. Go to step 8.

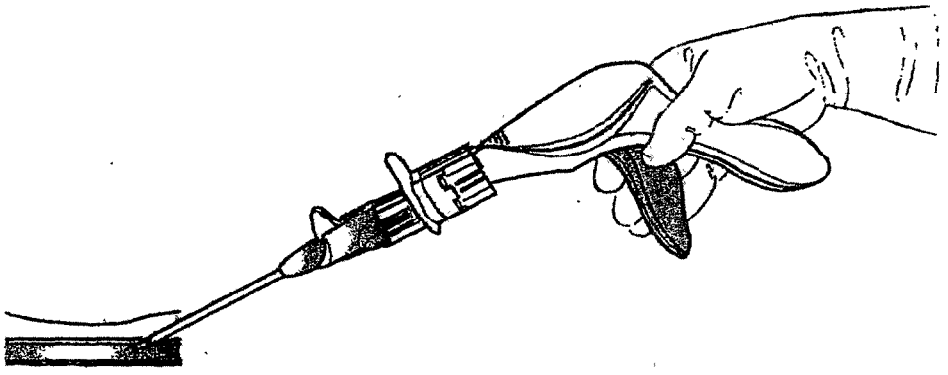
2. Use conventional compression methods to achieve hemostasis.



8. Locate the insertion point for the stapler.



9. Insert the stapler into the introducer until an audible click confirms that the two components are locked.

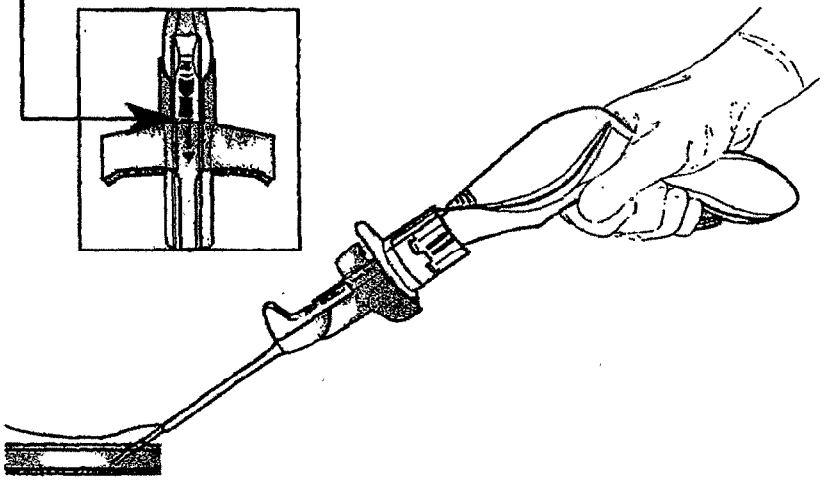


10. Raise the angle of the device to approximately 45 degrees or until resistance is felt from the surrounding tissue/skin. Squeeze the trigger completely. Ensure that you see green on the **NUMBER 4** indicator, signifying it is safe to remove the entire unit.

If green is not seen on the **NUMBER 4** indicator, ensure that the trigger is fully activated, and push the **NUMBER 4** lever distal to the instrument until green is fully visible.

Remove the device and discard.

Hold the groin for 2 minutes to ensure hemostasis has been achieved, and to control oozing from the subcutaneous tract.



STORAGE, PACKAGING AND DISPOSAL

The EVS ™ Vascular Closure System contains materials that are degraded by heat and moisture; therefore, the device must not be re-sterilized, and should not be stored at temperatures above 54° Celsius (130°F).

Sterile in unopened and undamaged package.

Dispose of the contaminated device, components, and/or packaging materials using standard hospital procedures and universally accepted practices for bio-hazardous wastes.

PRODUCT INFORMATION DISCLOSURE

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This product and its use is protected by US Patent Nos. 6,322,580, 6,348,064, 6,506,210, 6,533,762, 4,973,493, 4,979,959, 5,002,582, 5,263,992, 5,512,329, 5,714,360, and other patent(s) pending.

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